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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/441,140	11/16/1999	BEKA SOLOMON	SOLOMON1REI	3910

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EXAMINER	
BALLARD, KIMBERLY	

ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/441,140	SOLOMON, BEKA	
	Examiner	Art Unit	
	Kimberly A. Ballard	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2012*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *219-228* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *219-228* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

1. A decision of affirmed-in-part was given by the Board of Patent Appeals and Interferences on August 6, 2012. In the amendment filed August 16, 2012, Applicant canceled claims 177 and 210-218. Following the amendment, claims 219-228 are pending in the present application.

2. Upon further consideration and careful review of the oral hearing transcript held on July 24, 2012 (e.g., p. 14+) and the Board decision (mailed August 6, 2012) regarding written description (e.g., pp. 15-20), prosecution in this application has been reopened pursuant to 37 CFR 1.981. Claims **219-228** are under examination in the current office action.

Reissue Applications

3. Applicant is reminded of the continuing obligation under 37 CFR 1.178(b), to timely apprise the Office of any prior or concurrent proceeding in which Patent No. 5,688,651 is or was involved. These proceedings would include interferences, reissues, reexaminations, and litigation.

Applicant is further reminded of the continuing obligation under 37 CFR 1.56, to timely apprise the Office of any information which is material to patentability of the claims under consideration in this reissue application.

These obligations rest with each individual associated with the filing and prosecution of this application for reissue. See also MPEP §§ 1404, 1442.01 and 1442.04.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 219-228 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claim 219-221 and 225-227 are drawn to a therapeutic composition comprising a carrier and a genetically-engineered antibody, or binding fragment thereof, that binds beta-amyloid and disaggregates an aggregate of β-amyloid, wherein the antibody is obtained by genetically engineering the DNA encoding a monoclonal antibody that (i) binds and disaggregates β-amyloid and (ii) is obtainable using an immunogen consisting of Aβ1-28 or else recognizes an epitope within residues 1-28 of β-amyloid. Claims 222-223 are directed to a composition comprising a human monoclonal antibody, or binding fragment

thereof, that binds beta-amyloid and disaggregates an aggregate of β-amyloid, and which is obtainable using an immunogen consisting of Aβ1-28. And claims 224 and 228 are drawn to a method of making a therapeutic composition comprising a carrier and a genetically-engineered antibody, or fragment thereof, that binds beta-amyloid and disaggregates an aggregate of β-amyloid, comprising: selecting a monoclonal antibody that (i) binds and disaggregates β-amyloid aggregates and (ii) is obtainable using the immunogen Aβ1-28 (or that recognizes an epitope within residues 1-28 of Aβ); genetically engineering the DNA encoding said selected monoclonal antibody so as to produce a genetically-engineered antibody; and formulating the antibody with a pharmaceutical carrier. The claims thus encompass a genus of antibody molecules, or the production of such antibody molecules, which are claimed by desired functional properties.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. Applicants are directed to the recently-published guidelines on interpretation of the written description requirement, available on the internet at: http://www.uspto.gov/web/menu/written.pdf . See in particular Examples 10 and 14, drawn to a product claimed by its function and antibodies to a genus of proteins, respectively.

The recitation of a genetically-engineered antibody (or human monoclonal antibody) provides only a broad structural limitation, in that the claimed subject matter is directed to antibodies, which are proteins. This only limits the claimed subject matter to a broad structural class of molecules. The recitation of binding to beta-amyloid and disaggregating an aggregate of β-amyloid represents functional characteristics. There is no indication of any specific structural or physical properties of the claimed antibodies other than that they are antibodies. The indicated immunogen and/or epitope of the beta-amyloid peptide (Aβ1-28) does not provide a structural limitation for the antibodies, as the antigen-binding regions of the antibodies that are capable of being produced against this immunogen or that recognize an epitope within this region vary widely in terms of structure. There is no structure/function correlation provided, for example, between the desired epitope and the sequence corresponding to the antigen-binding (hypervariable) region of the antibody. What limited guidance is provided is generic and functional in nature, indicating only that the antibody should “bind to an epitope on the target molecule which is a region responsible for folding or aggregation” (column 5, lines 30-32). However, this does not impart any recognizable structure for the claimed antibody molecules. And apart from a method step to select for antibodies displaying the particular desired functional characteristics, there is no indication of any specific structural properties required for making the claimed genetically-engineered antibodies. There is not even identification of any particular portion of the antibody that must be conserved.

Moreover, the specification does not provide any examples of a species that falls within the claimed genus of antibody molecules. Neither of the disclosed anti-beta-amyloid monoclonal antibodies, AMY-33 or 6F/3D, are evidenced by the instant specification or the evidence of record as possessing the required functional limitation of disaggregating an aggregate of beta-amyloid (see also the TABLE provided by applicant at, for example p. 39 of the Appeal Brief filed 11/10/2010). Importantly, the specification does not recognize any antibody that is capable of binding beta-amyloid and disaggregating already aggregated beta-amyloid consistent with the claimed molecules. The anti-aggregation assay used to evaluate the effects of the AMY-33 and 6F/3D monoclonal antibodies on beta-amyloid (Example 22) is limited to determining the capacity to inhibit aggregation of beta-amyloid, and does not demonstrate disaggregating an aggregate of beta-amyloid as claimed. In other words, no species within the claimed genus of antibody molecules are proffered by the present disclosure. Consequently, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus nor guidance as to which of the myriad of antibodies and antibody fragments are encompassed by the claimed invention.

In view of the foregoing, the composition claims of claims 219-223 and 225-227 are considered to be “reach through” claims in that the specification hypothesizes the antibody’s existence and posits a screening assay which could be performed to order to identify disaggregating molecules having the ability to

dissolve already-aggregated proteins (column 5, lines 23-29). Here, applicant has not described the structures of a representative number of species of the genus now claimed, but rather has presented the public with an idea of how to perform an assay that might identify some agents that fall within the scope of the claim.

The instant composition claims are often referred to as "reach-through" claims, where an applicant attempts to obtain patent protection on an invention not yet discovered. The Court of Appeals for the Federal Circuit addressed claims of this sort in great detail in *University of Rochester v. G.D. Searle and Co.* (69 USPQ 2nd 1886, CAFC 2004). In *Rochester*, the Federal Circuit upheld the district court's ruling that patent claims which recited administration of compounds not disclosed, but rather to be identified in a screening assay, were invalid on their face. While the instant claims are drawn to therapeutic compositions comprising antibodies rather than methods of administering them, the situation is still analogous to that in *Rochester*. Since the specification does not disclose to the public the antibodies as claimed, it does not meet the written description requirement of 35 U.S.C. 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Additionally, in view of the statements by the Board of Patent Appeals and Interferences at pp. 19-20 of the Decision on Appeal (mailed August 6, 2012), the instant situation is directly analogous to that of *Centocor Ortho Biotech, Inc. v. Abbott Laboratories*, 636 F.3d 1341, 1351 (Fed. Cir. 2011) in that in *Centocor* the claims were drawn to antibodies in which the antigen of interest was known, but there was no description in the specification or prior art of the specific properties required. Similarly, in the instant case, there is no description of any "genetically-engineered" antibodies which bind β-amyloid and disaggregate an aggregate of β-amyloid.

The skilled artisan cannot envision the detailed chemical structure of the encompassed claimed antibodies or fragments thereof which bind to and disaggregate an aggregate of human beta-amyloid without further testing, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). Therefore, the full breadth of the claims does not meet the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. Claims 219, 220, 225 and 226 are rejected under 35 U.S.C. 102(a) as being anticipated by Walker et al. (*J. Neuropathol. Exp. Neurol*. 1994 Jul; 53(4):377-383; of record) as evidenced by Bard et al. (Proc. Natl. Acad. Sci. USA, 2003, 100(4):2023-2028; listed on IDS filed 12/19/2008). Note that a 35 U.S.C. 102 rejection over multiple references is proper when the additional references are cited to show that a characteristic not disclosed in the reference is inherent. See MPEP § 2131.01, section III.

Walker et al. teach a pharmaceutical composition comprising the monoclonal antibody 10D5 or Fab fragments thereof in sterile saline (see under "Injection of Antibody" at p. 378). As evidenced by Bard et al., the 10D5 antibody was raised against an immunogen consisting of Aβ1-28 (i.e., residues 1-28 of beta-amyloid) (see under "Monoclonal Antibodies (mAbs)" on p. 2023), and recognizes the epitope of Aβ3-7 (see Table 2 at p. 2026), which is within residues 1-28 of beta-amyloid. Also as evidenced by Bard, the 10D5 antibody is capable of binding to and removing (i.e., disaggregating) brain amyloid plaques, which would comprise aggregated beta-amyloid, both *ex vivo* (see Table 1 at p.

2024) and *in vivo* (see Fig. 4 at p. 2027). The sequence used to produce the 10D5 antibody was human beta-amyloid, and thus the 10D5 antibody binds human beta-amyloid as in claims 220 and 226. Hence, the pharmaceutical composition taught by Walker which comprises a pharmaceutically acceptable carrier (saline) and the 10D5 antibody are on point to the present composition claims in that the 10D5 antibody binds to beta-amyloid and is evidenced to be inherently capable of disaggregating an aggregate of beta-amyloid.

MPEP § 2112 provides guidance as to the Examiner's burden of proof for a rejection of claims under 35 U.S.C. 102 or 103 based upon the express, implicit, and inherent disclosures of a prior art reference. The case law clearly states that something which is old does not become patentable upon the discovery of a new property.

> "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999).

Thus, the claiming of a new use, new function or unknown property that is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). Further, the court has held that there is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355

F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention."); *Abbott Labs v. Geneva Pharms., Inc.*, 182 F.3d 1315, 1319, 51 USPQ2d 1307, 1310 (Fed.Cir.1999). Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established and the burden of proof rests upon the Applicant to demonstrate that the prior art does not necessarily or inherently possess the characteristics of Applicant's claimed product. *In re Fitzgerald*, 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977)). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Note that the preamble of "a therapeutic composition" does not confer patentable weight. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). See also

MPEP § 2111.02, section II. Moreover, it is noted that the antibody composition of Walker et al. is not inconsistent with therapeutic use.

Finally, the recitation of a "genetically engineered antibody [that] is obtained by genetically engineering the DNA encoding a monoclonal antibody" amounts to a product-by-process limitation and has not been accorded patentable weight. The process by which the claimed antibody is produced (i.e., "genetic engineering") does not in fact change the claimed product, which is still a composition comprising an anti-beta-amyloid antibody or binding fragment thereof. See MPEP § 2113, which states that:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

In other words, there is nothing to structurally or functionally distinguish the claimed antibody from that of the prior art monoclonal antibody taught by Walker. There is no limiting definition for "genetically-engineered" in the instant specification. Thus, the broadest reasonable interpretation would encompass, for example, recombinantly-produced antibodies which require genetically engineering the DNA encoding the antibody sequences such that they are produced in a host cell as part of the production process. However, the antibody thus produced would still necessarily comprise a structure (i.e., an amino acid sequence) identical to an antibody produced by other means, such as by obtaining it from a hybridoma. Regardless, any protein (including an antibody

made in a hybridoma) is encoded by DNA. It is also noted that the DNA in a hybridoma is considered recombinant as a result of the method of making the hybridoma. As noted by Judge Fredman of the Patent Trial and Appeal Board in the transcript of the oral hearing held 24 July 2012, it is reasonable to interpret the "genetically-engineered" limitations as product by process limitations. Accordingly, the teachings of Walker et al. provide for the presently recited invention of claims 219, 220, 225 and 226.

Conclusion

6. No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Ballard whose telephone number is (571)272-2150. The examiner can normally be reached on Monday-Friday 8:30 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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